REMARKS

Claims 19, 24, 25, 29 and 30 are pending in the application. In Paper No. 24, the Examiner has stated that the claims are subject to a restriction requirement, and asserts that claims 19, 24, 25 and 29 are constructively elected; therefore claim 30 is deemed to be withdrawn.

Claims 19, 24, 25 and 29 each stand rejected on various grounds under 35 U.S.C. § 102 and/or § 103.

I. Election/Restriction. → REMARKS

The Examiner has imposed a restriction requirement between claims 19, 24-25, and 29 and claim 30, asserting that claim 30 forms a "different group" in that it has an additional claim element (an adsorbent), which the Examiner asserts has not been previously searched or considered. On this basis, the Examiner contends that the inventions are distinct from each other.

The applicants respectfully traverse the imposition of this restriction requirement, and request rejoinder and examination of claim 30.

First, the Examiner has made no statement, other than a conclusory sentence, that the alleged separate inventions are independent or related and distinct, as required. M.P.E.P. 806. Moreover, the Examiner has not demonstrated that examination of claim 30 shall impose an undue burden upon him. Applicants note that, in the claims as originally filed, claim 1 encompasses within its scope a sample solution treating instrument having a control means that included an adsorbent, as presently claimed. See also claim 7, as originally filed. Accordingly, it is submitted that inasmuch as two Office Actions were issued in which claims 1 through 7 were examined, the Examiner has already conducted most if not all of any necessary search, and the burden imposed upon him by examination of claim 30 is not undue.

Accordingly, for at least these reasons, it is requested that the Examiner reconsider the imposition of the restriction requirement, and rejoin and examine claim 30.

II. Rejections Under 35 U.S.C. § 103(a) Based Upon Obata, Taken in View of U.S. Patent No. 6,183,740 or 5,935,442 (Claims 19, 24, 25).

The Examiner has rejected claims 19, 24, and 25 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,571,419 of Obata, *et al.* taken in view of newly cited references U.S. Patent Nos. 6,183,740 of Short, *et al.* ("Short") or 5,935,442 of Lihme, *et al.* ("Lihme"). As basis for the rejection, the Examiner asserts that Obata teaches the introduction of raw water into filtration units, the application of cation exchange, and the provision of the water to an acidic softened water tank where it is stored. The Examiner states that it is inherent that the pH of raw water is altered in some way in this tank. According to the Examiner, an oxidizing agent is added to the raw water through a pipe, the water is heated by a boiler, and is subsequently introduced into a reaction chamber where urea is decomposed by catalytic heat treatment. At the end of the process, water allegedly suitable for human consumption is obtained, and the Examiner asserts that a person tasting water is a biosensor.

The Examiner concedes that Obata does not teach the use of enzymes as a catalyst.

The Examiner attempts to remedy this deficiency by application of the disclosures of Short or Lihme, which allegedly teach use of biological enzymes in the bioconversion of potentially noxious substances, and water treatment wherein the active substance may be an enzyme, respectively.

The applicants respectfully traverse the rejection.

Relying on the Obata-Short or Lihme combination, the Examiner has failed to establish a *prima facie* case of obviousness. Obata teaches a method of producing pure water from urea-containing waste water. In the Obata process, once the water has been placed in the acidic softened water tank, it is tested, and if its pH is other than 3.0, the pH is adjusted using H_2O_2. See col. 7, line 3. Obata does not disclose consumption of water by humans, nor is there a disclosure of interference of urea in any "measurement results" allegedly obtained by a human biosensor. Moreover, as the Examiner concedes, Obata provides no teaching of use of an enzyme in the Obata method of decomposing urea from waste water.

Short, discloses a purified recombinant phytase enzyme derived from *Escherichia coli* B having a specific structure, and phytase activity. Short teaches that phytase enzymes, such as the claimed Short enzyme, are useful as supplements to phytate-containing foodstuffs, such as

grains, or legumes, that are to be fed to non-ruminants, to avoid the difficulties associated with high production of fecal matter containing a high concentration of minerals and elements. The Short disclosure teaches that the recombinant phytase described therein can be used in a method of hydrolyzing phytates. Substrates for the phytase includes foodstuffs, potential foodstuffs, ex-vivo reaction products and animal excremental products. Alternatively, Short teaches that the phytase enzyme may be administered to a non-ruminant animal, used in steeping cereals, the preparation of bread dough, and the preparation of Sake.

Lihme teaches a fluidized bed chromatographic process for the purification and binding of molecules in a liquid to an active substance covalently bound to a chromatographic adsorbent particles. The active substance that is covalently bound to the particles may be amino acid based polymer such as gelatin, albumin, hemoglobin, immunoglobin, antigens, protein G, lectins, glycoproteins, biotin binding proteins, avidin, streptavidin enzymes, proteases, and protease inhibitors. In an aspect of the invention, the particles are floated in waste water in order to purify or at least partly purify the water. Lihme teaches that in such situations the floating aspect of the particles is significant, as it confers the advantage of oxygen being available for, *e.g.*, micro-organisms growing in the interior of the conglomerate.

The combination of Obata and Short or Lihme does not render obvious the claimed invention. First, the combination does not teach or suggest each element of the invention. Neither Obata-Short or Obata-Lihme teaches or suggest a sample solution treating instrument having a control means for converting a sample solution to a condition for analysis by a biosensor that electrochemically measures a specific component in the sample solution. There is no biosensor disclosed in any of the three references. The Examiner contends that a "human tasting water" is interpreted as a biosensor in Obata. However, applicants point that out that (1) there is no teaching of a human consuming water in Obata or that such water is for human consumption; (2) a person "tasting" is not a process that electrochemically measures a specific component in water -- use of a human's gustatory apparatus is not the same as an electrochemical measurement.

Moreover, a person of skill in the art would not have had a motivation to combine the teachings of either Lihme or Short with those of Obata. Short teaches recombinant bacterial phytases, which are to be used in the breakdown of phytates (phytic acids). Lihme provides only

the general disclosure of "enzymes," but does not disclose use of the active substance covalently bound to chromatographic adsorbant particles, wherein the active substance is an enzyme for use in waste water treatment. Obata, in contrast, teaches use of a platinum catalyst for use in the breakdown of urea from waste water. Neither Lihme nor Short teaches removal or breakdown of urea using the phytases (Short), or the enzymes disclosed in Lihme (*e.g.*, glucose oxidase, proteases). Neither phytases nor proteases nor glucose oxidase are used to decompose urea. Thus, a person of skill in the art would have had no reason to make the combination of Obata with Lihme or Short, and therefore would have had no reasonable expectation that such combination would be successful as it would not result in a process that was useful in the breakdown of urea.

Accordingly, for at least these reasons it is respectfully requested that the Examiner reconsider and withdraw the rejection based upon the combination of Obata and Short or Lihme.

III. Rejection Under 35 U.S.C. § 103(a) Over U.S. Patent No. 5,378,635 (Claims 19 and 25).

The Examiner has rejected claims 19 and 25 under 35 U.S.C. § 103(a) asserting that they are unpatentable in view of U.S. Patent No. 5,378,635 ("Yasuda"). As basis for the rejection, the Examiner asserts that Yasuda teaches a method of measuring catecholamine including a sample pretreatment means and a sample dispensing means in the form of a syringe, which is coupled to the pretreatment means. The Examiner concedes that the reference does not teach that the sample pretreatment means is physically independent of the biosensor, but asserts that a person of skill in the art would have modified Yasuda by making the pretreatment means "separable" from the biosensing means. The applicants respectfully traverse the rejection.

Yasuda discloses a method of detecting catecholamines, such as dopamines, norephinephrine, and epinephrine by fluorescent labeling. The detection method disclosed in Yasuda involves the steps of (1) obtaining a biological sample and adding, *inter alia*, malemide to the sample prior to adding a fluorescence inducing reagent; (2) subsequently adding a fluorescence inducing reagent to the biological sample to obtain a "fluorescence inductor" (*i.e.*, a solution containing catecholamines with an activated fluophor; (3) supplying the fluorescence inductor to a microsyringe from which it is injected into a high speed liquid chromatographic

device; and (4) detecting the fluorescence intensity of the fluorescing catecholamines using a fluorometer. See, *e.g.*, Figure 1.

Yasuda does not teach or suggest each element of the invention for it does not describe a control means that includes an agent that is a catalyst or a buffer agent. When the sample solution is introduced into the microsyringe (which the Examiner asserts is the control means), it already contains both the maleimide and the fluorescence inductor.

Moreover, a person of skill in the art would not have been motivated to separate the microsyringe from the fluorometer by detaching it from the tubing, as suggested by the Examiner. The very purpose of the microsyringe attached to the fluorometer is to ensure efficient and clean, waste free introduction of the sample into the fluorometer. A person of ordinary skill would have had no motivation, based on the disclosure of Yasuda, to place the sample solution (already containing the maleimide and fluorescence inductor) into a syringe that is detached from the fluorometer, and subsequently set up tubing between the microsyringe and the fluorometer to inject the mixture into the fluorometer. Such a scenario is inefficient and a potentially wasteful process and there is no reason that the Examiner has pointed to that a person of skill would have undertaken to do so in practicing the method of Yasuda.

Accordingly, it is submitted that the Examiner's rejection has been overcome, and its reconsideration and withdrawal is respectfully requested.

IV. Rejection of Claims 19 and 25 Under 35 U.S.C. § 103(a) Based Upon U.S. Patent Nos. 5,262,305; 5,124,253; and 4,431,507 (Claims 19 and 25).

The Examiner has asserted that claims 19 and 25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,262,305 of Heller, *et al.* ("Heller"), U.S. Patent No. 5,124,253 of Foulds, *et al.* ("Foulds"), or U.S. Patent No. 4,431,507 of Nankai, *et al.* ("Nankai"), each taken individually. As basis for the rejection, the Examiner contends that, although each admittedly discloses a biosensor coupled to the alleged control means, it would have been obvious to a person of skill in the art to modify each of the disclosures by separating the biosensor from the remaining apparatus.

The applicants respectfully traverse the rejection.

Heller discloses a biosensor having an electrode substantially covered by a "sensing layer," and, on top of the sensing layer, an "interferent eliminating layer," consisting of a catalyst that is capable of oxidizing, and thereby eliminating, interfering substances, and a third outer layer "an oxidant generating layer." See, *e.g.*, Figure 3. The Heller layered electrode may be placed in a cell to which a sample solution is added, or it may be inserted into the sample solution.

Foulds discloses a dry strip element to be used in an electrochemical assay method for detecting theophylline in human biological fluids. The element is made up of a working electrode and a reference electrode. At the working electrode is an alkaline phosphatase and an electroinactive phosphate ester. The dry strip element may also incorporate a buffer having a pH of 9 to 10, and the buffer is positioned between the region of the sample solution and the alkaline phosphatase. Foulds teaches that one may incorporate into the test element, isoenzymes to remove any alkaline phosphotases indigenous to the sample that may reduce the desired substrate prior to the detection reaction, but will not interfere with the detection reaction itself.

Nankai discloses an improved enzyme electrode that is made up of a first electrode having one or more enzymes immobilized upon it and a second electrode that functions to remove materials that may interfere with the detection to be carried out by the first electrode. To accomplish electrochemical detection using this electrode, both the first and the second electrode are submerged in the test solution. The second electrode serves to electrochemically oxidize any interfering substances as the detection is accomplished by the first electrode.

None of these three references considered individually renders the claim invention obvious. First, as the Examiner has conceded, none teaches or suggests each element of the invention as claimed. Each discloses an apparatus that is integral to that portion of the apparatus that carries out the detection or measurement reaction.

Moreover, a person of skill in the art would have had no motivation to make the modification suggested by the invention. First, in all three references, separation of the measurement/detection portion of the disclosed apparatus would either be technically non-productive, or would render the disclosed apparatus not useful for the application for which it was intended. In the case of Heller, the Heller "intereferent eliminating layer" is sandwiched underneath the sensing layer and the oxidant generating layer. Separation of the bottom layer

(the sensing layer) from the layered sandwiched electrode would disrupt the ordered treatment of the sample as it flows through the sandwiched electrode, and therefore destroy the aim of Heller.

In the case of Foulds, the isoenzymes that remove undesirable alkaline phophastases are incorporated within the material of the test strip; therefore, separation of the isoenzymes from the test element would be unfeasible and impracticable, and a person of skill would not have been motivated to do so. Similarly, Nankai focuses on dual electrodes in close proximity wherein the first electrode electrochemically oxidizes interfering substances as the sample flows to the second electrode. Similar to the situation in Heller, a person of ordinary skill would not have been motivated to separate the two electrodes, as separation would disrupt the desired sequence of pretreatments in Nankai.

In the present invention, the separation of the pre-treating means from the biosensor is advantageous in that it permits more flexibility and adaptability of the pre-treating means. If the pre-treating means is integrated with the biosensor (as is true in the case of the prior art) it is capable of acting exclusively on a specific interfering substance only. Accordingly, the nature and type of interfering substance that may be removed by the pre-treating means (and subsequently not detected by the biosensor) is limited. Therefore, a specific biosensor coupled to a specific pre-treating means has limited and restricted utility. Use of the present invention solves this problem in that an appropriate pre-treating means can be selected regardless of the nature of the sample and/or the nature or mechanism of the biosensor to which the sample is to be submitted. Moreover, in the prior art, the pre-treating means merely acts on the specific interfering substance. Thus, it is necessary to modify the biosensor entirely to measure a sample solution that may contain other interfering substances.

For at least these reasons, a person of skill in the art would not have been motivated to make the modifications suggested by the Examiner of each of the above discussed references.

Accordingly, it is requested that the Examiner reconsider and withdraw the rejection.

V. Rejection Under 35 U.S.C. § 103(a) Over Obata, Taken in View of Short or Lihme, and Further in View of U.S. Patent No. 5,945,345.

The Examiner has rejected claim 29 under 35 U.S.C. § 103(a) as being unpatentable over Obata, considered in view of Short or Lihme, further taken in view of U.S. Patent No. 5,945,345

of Blatt. The Examiner applies the Obata and Short or Lihme combination as discussed above, and adds the disclosure of Blatt for its teaching of an "elastic sample supply means." In particular, the Examiner asserts that Blatt discloses a sample pad made of nylon, which the Examiner asserts is inherently "elastic" or "stretchable."

The applicants respectfully traverse this rejection.

Obata, Short and Lihme are described above.

Blatt discloses a filter for effectively removing substances from a sample of bodily fluid. Blatt teaches that the Blatt filter can be incorporated into assay devices which use a wicking member or transport matrix which is a porous material through which the test sample can easily pass. Blatt discloses that the porous material may be a nylon pad for use in a pour and flow through assay device having multiple layers for multiple assay reagents.

The combination suggested by the Examiner does not render obvious claim 29. The deficiencies, and non-combinability of Obata, Short or Lihme are discussed above, and relied upon herein. Moreover, as the Examiner concedes, none of these references teaches an elastic sample supply means. Blatt does not remedy this deficiency. The nylon pad of Blatt for use in a pour and flow through assay device is a porous material. There is no teaching or suggestion in Blatt that it is elastic in nature. The Examiner asserts that the material nylon is inherently "stretchable" and therefore Blatt describes this element inherently. To the contrary, under the doctrine of inherency it is not enough that the Blatt nylon pad may be elastic, it must necessarily be so. As would have been known to a person of skill in the art, the elasticity or stretchability of a given material is determined by many factors, including the weave or configuration of the fibers composed of the chemical material, the size, shape, and other physical aspects of the arrangement of the fibers of the material. Accordingly, there is no evidence that Blatt teaches an elastic supply unit.

Therefore, for at least these reasons, it is respectfully requested that the Examiner reconsider and withdraw the rejection of claim 29 over this combination.

CONCLUSION

In view of the foregoing, it is respectfully submitted that claim 30 should be rejoined and examined, and claims 19, 24, 29 and 30 are patentable over the cited prior art. Reconsideration and allowance of all pending claims at the earliest opportunity is respectfully requested.

Respectfully submitted,

MARIKO MIYASHITA, *et al.*

29 october 2003 By: Kristyne A. Bullock
(Date)

KRISTYNE A. BULLOCK
Registration No. 42,371
AKIN GUMP STRAUSS HAUER & FELD LLP
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103-7013
Telephone: 215-965-1200
Direct Dial: 215-965-1348
Facsimile: 215-965-1210
E-Mail: kbullock@akingump.com

KAB:cmb
7077516